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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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 EXAMINER

ART UNIT	PAPER NUMBER
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DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)
	09/341,079	FRESCO ET AL.
	Examiner	Art Unit
	John S. Brusca	1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM
THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 24 May 2001.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-32 is/are pending in the application.
 - 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-32 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 - a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) Interview Summary (PTO-413) Paper No(s) _____
- 5) Notice of Informal Patent Application (PTO-152)
- 6) Other _____

DETAILED ACTION

1. The instant application has been reassigned to a new examiner.
2. The marked up copy of the claims in the amendment received 24 May 2001 was defective in that in claims 31 and 32 the phrase "enhances triplex by effectively decreasing the amount of water at the site of triplex formation" was not indicated as an insertion by underlining. In addition the period of the sentence was improperly placed after "formation" instead of after "strand." The appropriate corrections to the marked up copy of the claims have been made by the examiner to clarify the amendment.

Specification

3. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Objections

4. Claims 31 and 32 are objected to because of the following informalities: The phrase "enhances triplex" should be amended to recite "enhances triplex formation.". Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of enhancing stability of triplex nucleic acids in an isolated solution, does not reasonably provide enablement for a method for enhancing stability of triplex

Art Unit: 1631

nucleic acids within a living cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation." These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

- a) In order to practice the full scope of the claimed invention one of skill in the art must make and use triplex nucleic acids within a cell whose stability is enhanced by addition of a water structure-making substance to the triplex nucleic acid within a cell. For the reasons discussed below, there would be an unpredictable amount of experimentation required to make and use the claimed invention.
- b) The specification presents no specific guidance for using the claimed method within a cell. The specification defines the term "solution" on page 5 of the instant specification as including both *in vitro* and *in vivo* environments
- c) The specification presents no working examples for using the claimed method within a cell.
- d) The invention is drawn to a method for enhancing stability of triplex nucleic acids within a living cell.

e) A review of the prior art does not reveal publications that provide guidance or working examples to practice the claimed method of enhancing stability of triplex nucleic acids within a cell.

f) The skill of those in the art of triplex nucleic acids is high.

g) The prior art is silent on the predictability of practicing the claimed invention within a cell.

h) The claims are broad in that they are drawn to methods of enhancing stability of triplex nucleic acids within a living cell by addition of a wide range of water structure-making substances to the cell, without any guidance as to how to add such water structure-making substances to a living cell, and without evidence that addition of such water structure-making substances would be effective and non-toxic to the cell if added to the cell.

The skilled practitioner would first turn to the instant specification for guidance in practicing the full scope of the claimed invention. However, the specification does not provide guidance or working examples to practice the claimed method within a living cell. As such, the skilled practitioner would turn to the prior art for such guidance, however the prior art does not show use of the claimed method within a living cell. Finally, said practitioner would turn to trial and error experimentation to practice the claimed method within a living cell. Such represents undue experimentation.

7. Claims 1-15, 31, and 32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to a method of adding a water

Art Unit: 1631

structure-making substance in greater than a stoichiometric amount to stabilize a triplex nucleic acid. The specification does not describe addition of water structure-making substances in greater than a stoichiometric amount.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 32 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claim 32 recites the limitation "the greater than a stoichiometric amount of the water structure-making substance." There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

11. The rejection of claims 1, 6, 14, 16, 21, 29, 31, and 32 under 35 USC 102(a) as being anticipated by Robles in the Office action mailed 21 November 2000 is withdrawn in view of the arguments presented in the amendment received 24 May 2001.

12. The rejection of claims 1, 11-14, 16, and 26-29 under 35 USC 102(b) as being anticipated by D'Souza et al. in the Office action mailed 21 November 2000 is withdrawn in view of the arguments presented in the amendment received 24 May 2001.

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Art Unit: 1631

14. Claims 1, 2, 4, 5, 9, 14, 16, 17, 19, 20, 24, 29, 31, and 32 are rejected under 35

U.S.C. 102(b) as being anticipated by Kiyama et al. for reasons of record.

Regarding the newly added limitation of addition of a water structure-making substance in greater than a stoichiometric amount, Kiyama adds cetyltrimethylammonium bromide, which is a water structure-making substance, in figure 4, and in the discussion on page 458 at a concentration of 100 μ M, with a concentration of oligonucleotide of 5 μ M.

Applicant's arguments filed 24 May 2001 have been fully considered but they are not persuasive. The applicants state that the concentration of cetyltrimethylammonium bromide used by Kiyama et al. is too low to provide water structure-making activity, however the claimed invention does not require a particular concentration of a water structure-making substance, and the inherent property of cetyltrimethylammonium bromide as a water structure-making substance is sufficient to cause Kiyama et al. to anticipate the claimed invention.

15. Claims 1, 7, 8, 14-16, 22, 23, and 29-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Shimizu et al. for reasons of record.

Regarding the newly added limitation of addition of a water structure-making substance in greater than a stoichiometric amount, Shimizu et al. adds 100 mM sodium acetate and 1 μ M oligonucleotide in the experiments summarized in Table 1.

Applicant's arguments filed 24 May 2001 have been fully considered but they are not persuasive. The applicants argue the use of sodium chloride by Shimizu et al. does not meet the limitations of the claimed invention, however Shimizu et al. adds sodium acetate to triplex nucleic acids, and therefore anticipates the claimed invention. Acetate is defined as a water structure-making substance on page 3 of the instant specification.

Art Unit: 1631

16. Claims 1, 11-16, and 26-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Moser et al..

The claims are drawn to a method of stabilization of a triplex nucleic acid by addition of ethanol or a cation that is not an alkali or alkaline earth metal cation.

Moser et al. shows use of hexamine cobalt cations (a transition metal) and ethanol to enhance the stability of triplex nucleic acids comprising derivatized nucleotides, detailed in Figure 5A and the second column of page 648.

17. Claims 1, 6, 14, 16, 21, 29, 31, and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Spink et al.

The claims are drawn to a method of stabilization of a triplex nucleic acid by addition of polyethylene glycol.

Spink et al. shows stabilization of triplex nucleic acids by addition of polyethylene glycol in figure 1.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca, Ph.D. whose telephone number is (703) 308-4231. The examiner can normally be reached on Monday -Friday 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward can be reached on (703) 308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 746-5137 for regular communications and (703) 746-5137 for After Final communications.

Art Unit: 1631

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

John S. Brusca
John S. Brusca, Ph.D.
Primary Examiner
Art Unit 1631

jsb
August 10, 2001